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From the
INTERNATIONAL SEARCHING AUTHORITY

To:

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PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY
(PCT Rule 43*bis*.1)

Applicant's or agent's file reference see form PCT/ISA/220	Date of mailing *(day/month/year)* see form PCT/ISA/210 (second sheet) **FOR FURTHER ACTION** See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/IB2004/001424	06.05.2004	06.05.2003

International Patent Classification (IPC) or both national classification and IPC
A61K9/22

Applicant
RANBAXY LABORATORIES LIMITED

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☒ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☒ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notifed the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:	Authorized Officer
European Patent Office - P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Pays Bas Tel. +31 70 340 - 2040 Tx: 31 651 epo nl Fax: +31 70 340 - 3016	VON EGGELKRAUT, S Telephone No. +31 70 340-4732

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/IB2004/001424

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was field, unless otherwise indicated under this item.

   ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material:

   ☐ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material:

   ☐ in written format

   ☐ in computer readable form

   c. time of filing/furnishing:

   ☐ contained in the international application as filed.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

Box No. II Priority

1. ☒ The following document has not been furnished:

   ☒ copy of the earlier application whose priority has been claimed (Rule 43*bis*.1 and 66.7(a)).

   ☐ translation of the earlier application whose priority has been claimed (Rule 43*bis*.1 and 66.7(b)).

   Consequently it has not been possible to consider the validity of the priority claim. This opinion has nevertheless been established on the assumption that the relevant date is the claimed priority date.

2. ☐ This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43*bis*.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.

3. Additional observations, if necessary:

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 27 and 28 with respect to industrial applicability

because:

☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination *(specify)*:

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for the whole application or for said claims Nos. 27 and 28 with respect to industrial applicability

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form	☐	has not been furnished
	☐	does not comply with the standard
the computer readable form	☐	has not been furnished
	☐	does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See separate sheet for further details

Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-28
	No:	Claims	
Inventive step (IS)	Yes:	Claims	2-5,23
	No:	Claims	1,6-22,24-28
Industrial applicability (IA)	Yes:	Claims	1-26
	No:	Claims	

2. Citations and explanations

see separate sheet

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

III. Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1

1.1 Claims 27 and 28 relate to subject-matter ("in-vivo release") considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).

V. Re Item V

Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

For the assessment of the present claims 27 and 28 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

2 Reference is made to the following documents:

D1 : WO 01/91716 A (HOOGEVEST PETER VAN ;KOHLMEYER MANFRED (CH); ADD ADVANCED DRUG DEL) 6 December 2001 (2001-12-06)

D2 : WO 01/47500 A (BEYERINCK RONALD ARTHUR ;CURATOLO WILLIAM JOHN (US); FRIESEN DWAYN) 5 July 2001 (2001-07-05)

3 INDEPENDENT CLAIM 1

3.1 The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claim 1 does not involve an inventive step in the sense of Article 33(3) PCT.

3.2 The document **D1** is regarded as being the closest prior art to the subject-matter of claim 1, and discloses (the references in parentheses applying to this document): An osmotic pressure driven monocompartment tablet comprising glipizide, microcrystalline cellulose, vinylpyrrolidone/vinyl acetate, polyethylene glycol, sodium chloride, magnesium stearate and a coating of two different cellulose acetates, polyethylene glycol and hydroxypropylmethylcellulose, having a passage through the coating.

3.3 The subject-matter of claim 1 therefore differs from this known composition in that at least one alginic acid derivative is comprised in the core.

3.4 The problem to be solved by the present invention may therefore be regarded as providing an alternative glipizide composition.

3.5 In view of D2 the solution proposed in claim 1 of the present application cannot be considered as involving an inventive step (Article 33(3) PCT) for the following reasons: Document D2 discloses monocompartment tablet comprising a low-solubility drug and a swellable composition. Sodium alginate is proposed as swelling agent. Osmotic active agents may be comprised in the tablet. The coating is semipermeable and has at least on delivery port. Glipizide is mentioned (page 13, line 30).

3.6 The features disclosed in D1 and D2 would be combined by the skilled person, without exercise of any inventive skills in order to solve the problem posed, as a matter of routine experimentation. The proposed solution in independent claim 1 thus cannot be considered inventive (Article 33(3) PCT).

3.7 The same reasoning applies, mutatis mutandis, to the subject-matter of the

corresponding independent claims 24 and 27, which therefore is also considered not inventive.

4 Dependent claims 6-22, 25, 26, 28 do not contain any features which, in combination with the features of any claim to which they refer, meet the requirements of the PCT in respect of inventive step, see document D1 and the corresponding passages cited in the search report.

5 The combination of the features of dependent claims 2-5, 23 is neither known from, nor rendered obvious by, the available prior art. The reasons are as follows: None of the prior art discloses or suggests a composition as claimed having a core comprising glipizide, an alginic acid derivative, an alkali metal or alkali earth metal as defined in claim 2 or more specifically being magnesium hydroxide or magnesium oxide, an inert excipient, a semipermeable membrane around said core and a passageway in the said membrane, nor is such a composition comprising sorbitol in the core suggested.

VIII. Re Item VIII
Certain observations on the international application

6 The application does not meet the requirements of Article 6 PCT, because claims 2, 4, 5, 24, 27 and 28 are not clear.

6.1 Claims 27 and 28 do not meet the requirements of Article 6 PCT in that the matter for which protection is sought is not clearly defined. The claims attempt to define the subject-matter in terms of the result to be achieved, namely achieving a biphasic release, which merely amounts to a statement of the underlying problem, without providing the technical features necessary for achieving this result.

6.2 The terms "light magnesium oxide" and "heavy magnesium oxide" used in claims 2, 4, 5 are vague and unclear and leave the reader in doubt as to the meaning of the technical features to which they refer, thereby rendering the definition of the subject-matter of said claims unclear, Article 6 PCT.

6.3 Claim 24 does not meet the requirements of Article 6 PCT in that the matter for which protection is sought is not clearly defined. The functional statement "an alkali metal or alkali earth metal as pH modifier" does not enable the skilled person to determine which technical features are necessary to perform the stated functions.

6.4 The vague and imprecise statement in the description on page 13, lines 8-10 and page 16, last paragraph implies that the subject-matter for which protection is sought may be different to that defined by the claims, thereby resulting in lack of clarity (Article 6 PCT) when used to interpret them.

7 Claims 24-26 are not supported by the description as required by Article 6 PCT.

7.1 Claims 24-26 are not supported by the description as required by Article 6 PCT, as their scope is broader than justified by the description. The reasons therefor are the following: The description provides support only for glipizide. No support is provided for a process involving any poorly soluble drug. Hence, claims 24-26 are not supported by the description as required by Article 6 PCT.